PEER REVIEW REPORT ON **MYCLOBUTANIL** 26.01.2009

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## 1. Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis

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| | Section 1<br>Data requirements: ***3***<br>Open points: ***6*** | | | Section 1<br>Data requirements: ***0***<br>Open points: ***0*** |
| | Open point 1.1<br>RMS to amend the list of end points to clarify the ratio of both enantiomers (preferably in the box "minimum purity").<br><br>See reporting table 1(5). | **DAS:** Noted | RMS has amended the LoEP.<br>As in the production process of myclobutanil neither stereo-selective reaction types nor enantiomerically pure substances are used, the myclobutanil obtained is a racemic mixture, i.e. 50:50 mixture of the two possible optical isomers. The nofier confirmed that there is no difference in biological activity between the two isomers. | PRAPeR 16 (13 – 16.03.2007):<br><br>Open point fulfilled. |
| | Open point 1.2<br>The criteria for accepting data on pourability should be discussed generally in a meeting of expert.<br><br>See reporting table 1(13). | **DAS:** as stated in column 3, point 1(13) of the Reporting Table, the pourability of the EW formulation (GF-1317) was to be investigated also in the shelf life study. This report (Report 04-407-G) was submitted on November 9th 2006 to RMS.<br><br>Within report: 04-407-G:<br>**Pourability:**<br>Initial: % residue was 5.7 and % rinsed residue was not determined<br>After storage: % residue was 4.0% and % rinsed residue was 0.2 | After 2 years of storage at ambient temperature, the residue was 4.0%. (See addendum to Vol.3(B2), dd. March 2007).<br><br>The initial residue (before storage) was determined to be 5.7% in study Tidswell (2004; ER 60.12), whereas in stability study Speak & Kendall (2004; ER 60.11; cfr. B.2.2.16) an initial residue of 4.7% was reported.<br><br>The criteria for accepting data on pourability should be discussed generally in a meeting of experts. | PRAPeR 16 (13 – 16.03.2007):<br><br>Open point fulfilled. |

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| 1.1 | Data requirement (for formal reasons)<br>The applicant should provide spectra for relevant impurity 14.<br><br>[This should be regarded as a technical data requirement since the data have been already submitted to the RMS]<br><br>See reporting table 1(15). | **DAS:** Noted | The requested spectra were submitted to the RMS and are considered acceptable (see addendum to Vol.3(B2), dd. March 2007); data requirement is considered to be fulfilled. | PRAPeR 16 (13 – 16.03.2007):<br><br>Data requirement closed. |
| | Open point 1.3<br>The acceptance of the study for the determination of the surface tension of myclobutanil should be discussed in a meeting of experts.<br><br>See reporting table 1(16). | **DAS:** indeed a higher purity is unlikely to change the surface tension value in a significative way. | As the purity of the test substance (i.e. 92.1%) is only slightly below the min. specified purity of the technical a.s. (i.e. 92.5%), the RMS considers the measured value to be representative for the technical a.s. as specified. Moreover, the conclusion on surface activity is very unlikely to change if a.s. of higher purity would be investigated, since there is a relative big difference between the trigger value (i.e. 60mN/m) and the measured value (i.e. 46.8 mN/m). | PRAPeR 16 (13 – 16.03.2007):<br><br>Open point fulfilled. |

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| | Open point 1.4<br>RMS to include the additional information concerning content of the relevant impurity in the formulation in an addendum or revised DAR.<br><br>The point is addressed, however, this additional information should be transferred into an addendum to the DAR, because of its importance.<br><br>See reporting table 1(17). | **DAS:** Noted | The additional information, i.e. the notifier's statement with regard to content of relevant impurity in the formulation, has been transferred into an addendum to Vol.3(B2), dd. March 2007 and has been included in the updated version of Vol.4(C), dd. March 2007. | PRAPeR 16 (13 – 16.03.2007):<br><br>Open point fulfilled. |
| 1.2 | Data requirement<br>A shelf life study must be provided.<br><br>[This should be regarded as a technical data requirement since the data have been already submitted to the RMS (November 2006]<br><br>See reporting table 1(20). | **DAS:** Noted. | Shelf life study was received (Kendall, 2006 – Report No. 04-407-G)<br>See addendum to Vol.3(B2), dd. March 2007. | PRAPeR 16 (13 – 16.03.2007):<br><br>Data requirement closed. |

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| | Open point 1.5<br>The acceptability of the analytical method for the determination of impurities in the technical material should be discussed in a meeting of experts.<br><br>See reporting table 1(30). | **DAS:** we confirm the justification reported in column 3, point 1(30) of the Reporting Table. | The notifier submitted following justification (June 2005):<br>*"The SANCO/3030/99 document specifies that the Horwitz test does not always apply. The Horwitz equation applicability to low levels at 0.1% or less is not straightforward as minor differences between first and second significant figures, although not different in practical, will make the Horwitz test fail. In addition, the SANCO/3030/99 document specifies a minimum of 5 samples. The data generated over two separate days will introduce more variability. In practical cases there is no difference between e.g. 0.020%, 0.019% and 0.022%. They all are 0.02%." "Furthermore, if we apply the test on one set and remove the day-day variability, the Horwitz test passes."*<br>The latter was demonstrated for one impurity, but appears not applicable to all impurities. However, it should be noted that in those cases, the Horwitz values are exceeded only slightly.<br>The RMS considers this justification acceptable. | PRAPeR 16 (13 – 16.03.2007):<br><br>Open point fulfilled. |

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| 1.3 | Data requirement (for formal reasons)<br>The applicant should provide additional validation data for the air method.<br><br>[This should be regarded as a technical data requirement since the data have been already submitted to the RMS]<br><br>See reporting table 1(32). | **DAS:** Noted | RMS considers the new analytical method, submitted by the notifier in August 2005, to be suitable for the determination of residues of Myclobutanil in air. See updated version of Vol.3(B5) dd. March 2007. | PRAPeR 16 (13 – 16.03.2007):<br><br>Data requirement closed. |
| | Open point 1.6<br>The acceptability of the analytical method used in storage stability studies with Synthane 20EW should be discussed in a meeting of experts.<br><br>See reporting table 1(33). | **DAS:** we confirm our justification reported in column 2, point 1(33) of the Reporting Table. | RMS considers the justification submitted by the notifier acceptable. | PRAPeR 16 (13 – 16.03.2007):<br><br>Open point fulfilled. |
| | Open point 1.7:<br><br>octanol/water coefficient to be discussed<br><br>See reporting table 1.7 | | | PRAPeR 16 (13 – 16.03.2007):<br><br>Open point fulfilled. |

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| | New open point 1.8:<br><br>RMS to amend the list of end points according to the discussion table. | | **RMS (June 2007)**<br>LoEP has been amended accordingly. | PRAPeR 16 (13 – 16.03.2007):<br><br>Open point still open.<br><br>Evaluation meeting (14-15.11.2007)<br><br>The end points have been amended and the open point is fulfilled. |

## 2 Mammalian toxicology

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| | Section 2<br>Data requirements: ***4***<br>Open points: ***14*** | | | Section 2<br>Data requirements: ***0***<br>Data gaps: ***0***<br>Open points: ***2*** |
| 2.1 | Data requirement (for formal reasons)<br>Applicant to submit the new ac toxicity package.<br><br>[This should be regarded as a technical data requirement since the data have already been submitted to the RMS.]<br><br>See reporting table 2(1). | **DAS:** Noted | See addendum.<br>The data requirement can be closed. | PRAPeR 19 (26. – 30.03.2007):<br><br>Data requirement fulfilled. |
| 2.5 | Data gap identified at PRAPeR 19:<br><br>Information on the comparability of the toxicological studies performed with technical material of different purity is required, as well a toxicological information on impurities. | | June 2007: QSAR was provided by the company for impurities 3 and 8 (see addendum). The analytical profile of batches used in tox studies was included in Vol 4, Annex C.<br>Impurity 8 is structurally comparable to the parent compound and will have probably a quite similar toxicitiy profile.<br>Impurity 3 has no structural alerts and is considered as not relevant by RMS.<br>RMS believes that the increase of | PRAPeR 19 (26. – 30.03.2007):<br><br>Data gap open.<br><br>Evaluation meeting (14-15.11.2007)<br>Data gap fulfilled |

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| | | | both impurities in the proposed specification should not change the toxicological properties of the parent compound. | |
| | Open point 2.1<br>RMS to assess and confirm the equivalence of the tox tested batches to the proposed technical specification.<br><br>See reporting table 2(1). | **DAS: The purity of the batches used for the Acute Toxicity Studies is 95.1 % and not 99.7% as confirmed by the relevant Certificate of Analysis included in the reports.** By mistake it was indicated by DAS in the submitted comment the purity of the reference standard instead of the technical material used. We confirm the batch used for the studies was originated by the actual source of tech. myclobutanil, KemFine. The validity of the reports and the relevant impact on the classification of the technical active substance should be revised taking into account this new context.<br>A brief summary of the Acute toxicity package is included as attachment to the Evaluation Table as word file:<br>**Appendix IV** to Evaluation Table section 2 | RMS proposes not to take this new package (summarized in the addendum) into account as the results of acute toxicity obtained with this new source present a lesser hazard compared to the reference source.<br>A high increase in purity (from 84% up to 95.1%) could affect the complete toxicology profile of the active ingredient and acute toxicity studies are not sufficient to address the hazard of myclobutanil taking into account the reproduction/developmental toxicity profile of this compound.<br>Further assessment of equivalence is considered necessary before to amend the proposed classsification.<br>This point could be closed.<br>June 2007: no further comments | PRAPeR 19 (26. – 30.03.2007):<br><br>Open point open.<br><br>Evaluation meeting (14-15.11.2007)<br>Open point still open |
| | Open point 2.2<br>The need of classification R36 “Irritating to eyes” to be discussed in an experts’ meeting | **DAS:** taking into consideration DAS comment at 2(1) and on the basis of the new acute toxicity data, myclobutanil should not be classified for acute toxicity.<br>The low incidence and severity of the eye irritation at 21 days may indicate that | RMS agrees. | PRAPeR 19 (26. – 30.03.2007):<br><br>Open point fulfilled. |

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| | See reporting table 2(2). | classification is not required, and this is further supported by the new eye irritation study in which only mild irritation was observed. | | |
| | Open point 2.3<br>The relevance of liver effects in the 90-day and 1-year studies in dog to be discussed in an experts' meeting.<br><br>See reporting table 2(7). | **DAS:** our comments are expressed in the document *"Position Document in response to EFSA/MSs comments (Reporting Table) on the Myclobutanil DAR"* point point 1) Effects in dog Livers, attached to the Evaluation Table as word file:<br>**Appendix I** to Evaluation Table section 2<br>The same document was addressed to the attention of RMS on September 7th, 2006. | The *"Position Document in response to EFSA/MSs comments (Reporting Table) on the Myclobutanil DAR"* point point 1) Effects in dog Livers, supports RMS proposal and is included in the addendum. | PRAPeR 19 (26. – 30.03.2007):<br><br>Open point fulfilled.<br>An overall subchronic NOAEL of 100 ppm was proposed (90 d and 1 y dog) |
| | Open point 2.4<br>Reproductive and developmental toxicity to be discussed in an experts' meeting<br><br>See reporting table 2(12). | **DAS:** our comments are expressed in the document "*Myclobutanil reprotox position paper*" attached to the Evaluation Table as word file:<br>**Appendix III** to Evaluation Table section 2<br>The same document was addressed to the attention of RMS on May 30th, 2006. | No comments | PRAPeR 19 (26. – 30.03.2007):<br><br>Open point fulfilled.<br><br>The meeting agreed that these findings do not warrant the classification with R 62. |
| | Open point 2.5<br>The issue of triazole metabolite is going to be discussed in a dedicated experts' meeting. Conclusions to be awaited.<br><br>See reporting table 2(17). | **DAS:** the toxicity studies on metabolites were supplied only for completion of information. TA occurs in wheat grain that we confirm is not an intended/defended use for myclobutanil. The conclusions of the dedicated expert meeting therefore have no direct relevance for the evaluation of myclobutanil. | No comments | PRAPeR 19 (26. – 30.03.2007):<br><br>Open point closed.<br><br>The notifier has withdrawn the use from the list of the intended uses. |

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| 2.2 | Data requirement (for formal reasons)<br>The applicant should provide a case and/or data to show that the increased levels of both impurities (3 and 8) will not have a significant adverse effect on the toxicity of technical Myclobutanil<br><br>[This should be regarded as a technical data requirement since the data have been already submitted to the RMS]<br><br>See reporting table 2(21) and 1(4) in section 1. | **DAS:** Noted | No comments | |
| | Open point 2.6<br>The relevance of impurities 3 and 8 to be discussed in an experts' meeting<br><br>See reporting table 2(21). | **DAS:** Noted | No comments<br>June 2007: see comments on data gap 2.5 | PRAPeR 19 (26. – 30.03.2007):<br><br>Open point open.<br><br>Evaluation meeting (14-15.11.2007)<br>Open point still open |
| | Open point 2.7<br>The relevance of metabolites RH-9090 (M4) and RH-9083 (M3) to be discussed in a | **DAS:** both metabolites are rat metabolites and therefore no additional studies are required. Please amend RH-9083 to RH-9089. | RMS agrees.<br>This point can be closed. | PRAPeR 19 (26. – 30.03.2007): |

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| | meeting of experts.<br><br>See reporting table 2(22). | | | Open point fulfilled. |
| 2.3 | Data requirement<br>Applicant to provide further information on health effects/surveillance programmes in manufacturing plant personnel<br><br>In the comments to the reporting table the applicant announced that a report covering medical surveillance in a manufacturing plant in Italy (2000-20005) was sent to the RMS.<br><br>See reporting table 2(23). | **DAS:** we confirm the report was sent to the RMS (November 29th, 2006) | RMS included the information in the addendum.<br>The point can be closed. | PRAPeR 19 (26. – 30.03.2007):<br><br>Data requirement fulfilled. |
| | Open point 2.8<br>AOEL to be discussed in an experts' meeting.<br><br>See reporting table 2(24). | **DAS**: In accordance with the current GAP for Systhane 20EW, a maximum of 4 applications can be made, during the fruit development season. The NOAEL should reflect adverse effects which are expected to occur during this time-frame. In summary, the 2-generation study NOAEL, with a safety factor of 100 gives an AOEL value of 0.16 mg/kg bw/day.<br>The critical subchronic effects observed | The comment of the company (included in the addendum) supports the RMS proposal. | PRAPeR 19 (26. – 30.03.2007):<br><br>Open point fulfilled. |

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| | | were hepatocellular changes in the 1-year dog study (following 1-year of exposure only) and reproduction effects in the 2-generation rat study.<br>90-D dog study NOAEL: 56.8 mg/kg bw/day.<br>1-Yr dog study NOAEL: 14.28 mg/kg bw/day.<br>2-Gen study NOAEL: 16 mg/kg bw/day.<br>In the 1-year dog study, changes in ALT were observed from the Week 25 clinical chemistry sample time-point but they did not worsen with increased exposure duration. As the adverse effects (hepatocytes ballooning) in the dog were only seen after one year at 1600 ppm, and not before 3 months (maximum exposure window), the NOAEL from the 2-generation study is appropriate to use for AOEL setting, and would adequately protect against any hepatic or testicular effects of concern.<br>The use of the 1-year NOAEL from the 2-year chronic rat study is inappropriate as the duration of exposure far exceeds that expected from use of the product. The LOAEL for the testicular effects was 39.2 mg/kg bw/day at 1-year. Similar effects at the 1-year NOAEL of 9.8 mg/kg bw/day were not observed until the 2-year time-point. The 2-generation reproduction study provides a >2-fold margin of safety | | |

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| | | compared to the 1-year LOAEL.<br>The appropriate safety factor for setting the AOEL is 100, as there is no justification for using a greater value. The testicular effect is an effect produced from prolonged exposure with a clear NOAEL, and a worker is not going to be exposed to myclobutanil persistently in order for any adverse effects to occur. The 3-month toxicity study in the rat did not show any testicular effects up to and including doses of 585 mg/kg bw/day. The severity of this chronic effect does not warrant an additional safety factor.<br>**In addition**, please refer to the document *"Position Document in response to EFSA/MSs comments (Reporting Table) on the Myclobutanil DAR"* point 2) Setting the AOEL, attached to the Evaluation Table as word file:<br>**Appendix I** to Evaluation Table section 2<br>The same document was addressed to the attention of RMS on September 7th, 2006. | | |
| | Open point 2.9<br>The ArfD to be discussed in an experts' meeting.<br><br>See reporting table 2(27). | **DAS:** our comments are expressed in the document *"Position Document in response to EFSA/MSs comments (Reporting Table) on the Myclobutanil DAR"* point 4) ARfD Setting, attached to the Evaluation Table as word file:<br>**Appendix I** to Evaluation Table section 2<br>The same document was addressed to | The position paper (included in the addendum) of the company supports the RMS proposal. | PRAPeR 19 (26. – 30.03.2007):<br><br>Open point fulfilled. |

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| | | the attention of RMS on September 7th, 2006. | | |
| | Open point 2.10<br>RMS to provide details on the existing classification of co-formulants and their impact on the classification of the preparation.<br><br>See reporting table 2(30). | **DAS:** about R65, is assigned when:<br>Liquid substances and preparations presenting an aspiration hazard in humans because of their low viscosity:<br>(a) for substances and preparations containing aliphatic, alicyclic and aromatic hydrocarbons in a total concentration equal to or greater than 10 % and having either:<br>- a flow time of less than 30 sec. in a 3 mm ISO cup according to ISO 2431, or<br>- a kinematic viscosity measured by a calibrated glass capillary viscometer in accordance with ISO 3104/3105 of less than 7 mm2/sec. at 40 °C, or<br>- a kinematic viscosity derived from measurements of rotational viscometry in accordance with ISO 3219 of less than 7 mm2/sec. at 40 °C.<br>Note that substances and preparations meeting these criteria need not be classified if they have a mean surface tension greater than 33 mN/m at 25 °C as measured by the du Nouy tensiometer or by the test methods shown in Annex V, Part A.5;<br>(b) for substances and preparations, based on practical experience in humans.<br>Systhane 20EW has a high viscosity and | RMS considers that classification of co-formulants and their impact on the classification of the preparation is not relevant for a Praper meeting. This discussion should be forwarded to ECB (ISPRA) where specialists are involved with classification and labelling.<br>This point could be closed. | PRAPeR 19 (26. – 30.03.2007):<br><br>Open point closed.<br><br>The classification and labelling of co-formulants and their impact on their impact on the classification of the preparation is not relevant for the PRAPeR expert meeting. |

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| | | surface tension therefore R65 is not triggered under any of the above criteria.<br>About R66<br>For substances and preparations which may cause concern as a result of skin dryness, flaking or cracking<br>but which do not meet the criteria for R38 based on either:<br>. practical observation after normal handling and use, or<br>. relevant evidence concerning their predicted effects on the skin.<br>This phrase is assigned not on study results but on practical evidence; Systhane 20 EW has been extensively used in the past and in the present with no adverse effects reported. We consider that R66 would not be appropriate. | | |
| | Open point 2.11<br>Dermal absorption to be discussed in an experts' meeting.<br><br>See reporting table 2(31). | | No comments | PRAPeR 19 (26. – 30.03.2007):<br><br>Open point fulfilled.<br><br>The revised values for dermal absorption are:<br><br>25%for the concentrate<br>15% for the dilution. |
| 2.4 | Data requirement (for formal | **DAS:** Noted | The new study is summarized in the | PRAPeR 19 (26. – 30.03.2007): |

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| | reasons)<br>Applicant to submit the new *in vitro* dermal study.<br><br>[This should be regarded as a technical data requirement since the study has already been submitted.]<br><br>See reporting table 2(35). | | addendum. Appropriate values were used in the new operator exposure assessment reported in the addendum.<br>This point could be closed. | Data requirement fulfilled. |
| | Open point 2.12<br>Input parameters for exposure assessment to be confirmed in an experts' meeting.<br><br>See reporting table 2(41). | **DAS:** please refer to the update of the operator exposure sent to the attention of RMS on September 20th, 2006. The mentioned document is attached to the Evaluation Table as word file:<br>**Appendix II** to Evaluation Table section 2 | June 2007: A new proposal is reported in the updated addendum post Praper 19.<br>Operator exposure is below the AOEL.<br>Open point can be closed.<br>. | PRAPeR 19 (26. – 30.03.2007):<br><br>Open point open.<br><br>Evaluation meeting (14-15.11.2007)<br>The point is fulfilled |
| | Open point 2.13<br>Bystander exposure to be discussed in an experts' meeting.<br><br>See reporting table 2(43). | **DAS:** please refer to the update of the operator exposure sent to the attention of RMS on September 20th, 2006. The mentioned document is attached to the Evaluation Table as word file:<br>**Appendix II** to Evaluation Table section 2 | A new proposal is reported in the updated addendum post Praper 19. Bystander exposure is below the AOEL.<br>Open point can be closed. | PRAPeR 19 (26. – 30.03.2007):<br><br>Open point open.<br><br>Evaluation meeting (14-15.11.2007)<br>The point is fulfilled |
| | Open point 2.14<br>Worker exposure to be | **DAS:** please refer to the update of the operator exposure sent to the attention of RMS on September 20th, 2006. The | A new proposal is reported in the updated addendum post Praper 19. Worker exposure is below the | PRAPeR 19 (26. – 30.03.2007): |

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| | discussed in an experts' meeting.<br><br>See reporting table 2(44). | mentioned document is attached to the Evaluation Table as word file:<br>**Appendix II** to Evaluation Table section 2 | AOEL.<br>Open point can be closed. | Open point open.<br><br>Evaluation meeting (14-15.11.2007)<br>The point is fulfilled |
| | Message from phys-chem to tox:<br><br>Message to tox, residues, fate and ecotox that the technical material is a racemic mixture and has this been considered in the risk assessment. | | | A statement was submitted by the notifier. The racemic mixture consists of two possible optic isomers in the ration 50:50.<br><br>This has not specifically considered. Provided the racemic mixture is stable the concern is covered by the tests performed. |

## 3 Residues

| No. | Column A<br>Conclusions of the EFSA Evaluation Meeting | Column B<br>Comments from the main data submitter / applicant on the EFSA Evaluation Meeting conclusion | Column C<br>Rapporteur Member State comments on main data submitter / applicant comments | Column D<br>Recommendations EPCO Expert Meeting / Conclusions of the Evaluation Meeting |
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| | Section 3<br>Data requirements: ***1***<br>Open points: ***27*** | | | Section 3<br>Data requirements: ***1***<br>Data gaps: ***3***<br>Open points: ***10*** |
| | Open point 3.1<br>RMS to present clarification on apple metabolism given in column 3 in an addendum<br><br>See reporting table 3(3). | **DAS:** Noted | The extraction procedure for apple juice and apple pomace is presented in the Addendum to the DAR – February 2007.<br>RMS agrees that the extractability figures for pomace in the text (DAR) may not be correct (based on the radioactivity level in the chloroform extract but should be based on the total residues recovered in the methanol extracts). | PRAPeR 20 (27. – 30.03.2007):<br><br>Open point fulfilled.<br><br>Clarifications provided in the Addendum to the DAR (February 2007) |
| | Open point 3.2<br>The study 'Laboratory metabolism studies of 14C RH-3866 in wheat' by Nelson, S.S. (1984) is considered as not acceptable for evaluation by RMS.<br>This should be highlighted in a revised DAR/addendum/corrigendum as appropriate, and the list of references relied upon in the DAR as well the list of information, tests and studies | **DAS:** Noted | The non reliability of this study was highlighted in the Addendum to the DAR – February 2007.<br>The list of references relied upon in the DAR as well the list of information, tests and studies considered relied upon were amended accordingly. | PRAPeR 20 (27. – 30.03.2007):<br><br>Open point fulfilled.<br><br>The study has been deleted from the list of studies relied upon. |

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| | considered relied upon should be amended accordingly.<br><br>See reporting table 3(5). | | | |
| | Open point 3.3<br>RMS to provide the missing TRR values for the wheat metabolism study in an addendum<br><br>See reporting table 3(6). | **DAS:** Noted | The TRR values in the methanol extracts were not provided.<br>Considering the general experimental design, this study is considered as unacceptable. | PRAPeR 20 (27. – 30.03.2007):<br><br>Open point fulfilled.<br><br>The study has been deleted from the list of studies relied upon. |
| | Open point 3.4<br>As recently concerns have been raised on the toxicological relevance of the triazole derivate metabolites (teratogenic and/or embryotoxic resp.) these aspect needs prudent consideration even if the use on cereals is currently not notified as a representative use (but may be in future on MS level)<br>As this metabolites are not specific to myclobutanil but to all triazole pesticides, a general solution with support of the toxicology meeting | **DAS:** we confirm that cereals are not a representative use. The conclusions of the dedicated expert meeting therefore have no direct relevance for the evaluation of myclobutanil. | This point was discussed in the PRAPeR 15 Expert Meeting.<br>Toxicological end points were determined for the triazole derivate metabolites (Triazole Acetic Acid and Triazole Alanine).<br>These metabolites were identified in the metabolic pathway of Myclobutanil in wheat.<br>Therefore, the proposition should be to include these 2 relevant metabolites in the definition of the residue for wheat grain both for monitoring and risk assessment.<br>If in the future, cereals become a representative use, the risk assessment will be performed by comparing the residue level of the | PRAPeR 20 (27. – 30.03.2007):<br><br>Open point fulfilled.<br>A general discussion of the triazole derivate metabolites issue took place in round 3 of PRAPeR meetings.<br>For myclobutanil: If in the future new uses other than fruits and cereals will be envisaged new metabolism studies might be necessary to address triazole derivate metabolites. |

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| | could be discussed in an experts' meeting<br><br>See reporting table 3(7). | | triazole derivate metabolites to their respective toxicological end points. | |
| | Open point 3.5<br>Updated list of studies relied upon to be provided as a clear indication of which of the available studies are considered acceptable and reliable for evaluation of the residue behaviour of myclobutanil<br><br>See reporting table 3(9). | **DAS:** Noted | An updated list of studies relied upon was included in the Addendum to the DAR – February 2007.<br>. | PRAPeR 20 (27. – 30.03.2007):<br><br>Open point fulfilled.<br><br>The updated list of studies relied upon was included in the Addendum to the DAR (March 2007) |
| | Open point 3.6<br>Information on the radioactive purity and the specific activity of the test substance to be provided in an addendum<br><br>See reporting table 3(10). | **DAS:** Noted | These data are presented in the Addendum to the DAR – February 2007. | PRAPeR 20 (27. – 30.03.2007):<br><br>Open point fulfilled.<br>Information has been provided in the Addendum to the DAR (March 2007). |
| | Open point 3.7<br>RMS to present clarification on grape metabolism following a foliar treatment given in column 3 in an | **DAS:** Noted | Clarifications on the grape metabolism are presented in the Addendum to the DAR – February 2007. | PRAPeR 20 (27. – 30.03.2007):<br><br>Open point fulfilled. |

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| | addendum<br><br>See reporting table 3(11). | | | Information has been provided in the Addendum to the DAR (March 2007). |
| | Open point 3.8<br>RMS to give clarification on apple metabolism study with regard to extractability and attempts to release, characterise and identify the non extractable residues in an addendum<br><br>See reporting table 3(12). | **DAS:** Noted | Clarifications on the apple metabolism are presented in the Addendum to the DAR – February 2007 under open point 3.1. | PRAPeR 20 (27. – 30.03.2007):<br><br>Open point fulfilled.<br><br>Information has been provided in the Addendum to the DAR (March 2007). |
| | Open point 3.9<br>RMS to present clarification on metabolism in laying hens given in column 3 in an addendum<br><br>See reporting table 3(16). | **DAS:** Noted | Clarifications on laying hens metabolism are presented in the Addendum to the DAR – February 2007 under open points 3.9/3.11. | PRAPeR 20 (27. – 30.03.2007):<br><br>Open point fulfilled.<br><br>Information has been provided in the Addendum to the DAR (March 2007), however this metabolism study is not required and should not be reported on the list of studies to be relied on |
| | Open point 3.10<br>Clarifying information on the metabolism study in cows addressing comments 3(19)-1 | **DAS:** Noted | Clarifications on the metabolism study in cows are presented in the Addendum to the DAR – February 2007. | PRAPeR 20 (27. – 30.03.2007):<br><br>New data gap: A ruminant metabolism |

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| | to 3(19)-7 to be presented in an addendum<br><br>See reporting table 3(19). | | RMS -June 2007 :<br>RMS disagrees on this new data gap. This was already pointed out in the Addendum – March 2007 peer reviewed during PRAPeR 20.<br>RMS is convinced that no further relevant information will be brought by a new ruminant metabolism study for the following reasons :<br>-although a mixture of $^{14}$Cphenyl-Myclobutanil and $^{14}$C-triazole RH-9090 and RH-9089 was used as a test substance, demonstration has been made that the phenethyl triazole linkage was not cleaved and therefore the triazole derivate metabolites are not expected to be recovered in the livestock matrices.<br>-it is true that the identification of the residues was rather low (40% TRR) in liver and kidney but at the calculated dietary burden, the residue levels in milk, muscle, fat and kidney were below the LOQ (0.005 mg/kg for milk and 0.02 mg/kg for tissues) of the analytical method and 0.045 mg/kg in liver (Table B.7.2.1-2 in the DAR).<br>-apple pomace cannot be considered as a highly relevant feed item for ruminants (10% and 30% of total DM/day, resp. for dairy and beef cattle).<br>Finally, the grapes use is not affected | study is required where the compound is labelled on both rings. |

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| | | | by this discussion. | |
| 3.2 | Data gap identified at PRAPeR 20:<br>A ruminant metabolism study is required where the compound is labelled on both rings. | | See open point 3.10 | PRAPeR 20 (27. – 30.03.2007):<br>Data gap open.<br>Evaluation meeting (14-15.11.2007)<br>Data gap open. |
| | Open point 3.11<br>Clarifying information on the metabolism study in hens to be presented in an addendum.<br>See reporting table 3(20). | **DAS:** Noted | Clarifications on laying hens metabolism are presented in the Addendum to the DAR – February 2007 under open point 3.9/3.11. | PRAPeR 20 (27. – 30.03.2007):<br>Open point fulfilled.<br>Information has been provided in the Addendum to the DAR (March 2007), however this metabolism study is not required and should not be reported on the list of studies to be relied on |
| | Open point 3.12<br>Proposed residue definition for food of animal origin and consideration of whether or not MRLs might be needed to be presented in an addendum<br>Justification for the resepective proposals should be given, taking into account | **DAS:** There are existing EU MRLs for myclobutanil in commodities of animal origin and they are based on RH-9090 (expressed as myclobutanil equivalents) as the residue definition. It is proposed that a residue definition in commodities be retained to support the existing MRLs even if the residue intake in in livestock based on | A) Metabolism studies in laying hens and lactating cows have been provided and can be considered as acceptable (demonstration has been made that the phenethyl triazole linkage was not cleaved and therefore the triazole derivate metabolites are not expected to be recovered in the livestock | PRAPeR 20 (27. – 30.03.2007):<br>Open point fulfilled for hen.<br>Open point still open for ruminants<br>Evaluation meeting (14-15.11.2007) |

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| | open point in 3(24) in terms of MRL proposlas and comments in 3(25) and 3(30) in terms of relevance of metabolites (potential of toxicity and/or fat solubility)<br><br>See reporting table 3(21). | representative crops is not sufficient to require MRLs. Additionally, it is proposed that a residue definition be established since, even if the dietary burden for the representative crops does not trigger the need for MRLs, crops and associated MRLs considered at a later time will result in the need for a residue definition in livestock commodities. | matrices).<br>B) The residue definition for monitoring and risk assessment is proposed as follows :<br>*Cows* : the metabolite RH-9090 expressed as myclobutanil equivalents.<br>*Poultry* : Myclobutanil + RH-9090 expressed as myclobutanil equivalents.<br>C) MRLs proposals can be proposed for ruminants matrices only according to the representative uses. A MRL of 0.01* mg/kg is proposed for milk, muscle, fat, liver and kidney although the DFG S19 analytical method is not suitable for the determination of RH-9090 in fat (mean recovery values were lower than 70 % and RSD values exceeded 20%).<br>RMS -June 2007 :<br>The proposed residue definition for monitoring and risk assessment for matrices of ruminants is the metabolite RH-9090 expressed as myclobutanil equivalents.<br>A MRL of 0.01* mg/kg is proposed for milk, muscle, fat, liver and kidney although the DFG S19 analytical | Open point still open for ruminants |

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| | | | method is not suitable for the determination of RH-9090 in fat (mean recovery values were lower than 70 % and RSD values exceeded 20%). | |
| | Open point 3.13<br>RMS to elaborate on the changed proposal for the residues definition for risk assessment (myclobutanil + RH 9090) in an addendum; consideration should be also given to a potential inclusion of RH-9089 depending on its toxicological relevance<br><br>See reporting table 3(22). | **DAS:** Levels of RH-9089 are not significant as stated in the comments from RMS in Column 3 of the Reporting Table at 3(22), 3(26) and 3(27) and from UK in the "Comments received on reporting Table, Section Residues" at 3(26) and 3(27). RH-9089 should not be included in the residue definition. | The metabolites RH-9090 and RH-9089 were recovered in the rat metabolism along with the parent compound and were shown to have a similar toxicity as the parent compound through metabolisation on the side chain of the parent molecule only suggesting a detoxification pattern.<br>Based on the available metabolism studies in grapes and apples, the parent Myclobutanil is the most relevant indicator for enforcement purposes while the metabolite RH-9090 should be included in the residue definition for risk assessment due to its similar toxicity to the parent compound.<br>The metabolite RH-9089 was recovered at a trace level in grapes and apples and therefore it was decided not to include it in the definition of residue for risk assessment. | PRAPeR 20 (27. – 30.03.2007):<br><br>Open point closed. |
| | Open point 3.14<br>RMS to elaborate on the question of whether the available metabolism study in cows can be used to derive a | **DAS:** Noted | RMS agrees that there is no evidence that the metabolites RH-9090 and RH-9089 recovered in the cow metabolism study are degradation products of myclobutanil since these metabolites were also used as test substances. | PRAPeR 20 (27. – 30.03.2007):<br><br>Open point closed |

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| | metabolic pathway and to confidently propose a residue definition in ruminants, respectively, in an addendum<br><br>See reporting table 3(23). | | It is also true that the rate of identification in liver and kidney is relatively low (30% and 40 % of TRR, respectively) to assess that the degradation pathway was completely investigated.<br>However, no cleavage of the phenethyl triazole linkage occurred in order to generate the toxicologically relevant triazole derivate metabolites and as it is observed in the rat metabolism, the degradation of myclobutanil took place essentially on the alkyl side chain of the parent molecule to provide exclusively compounds structurally related to myclobutanil.<br>For these reasons, a new metabolism study in lactating cows should not be required.<br>RMS -June 2007 :<br>RMS considers that a metabolic pathway can be depicted for ruminants considering the available metabolism study. A valid residue definition both for monitoring and risk assessment can be proposed. | See new data gap for a ruminant metabolism study. (data gap 3.2) |
| | Open point 3.15<br>RMS to verify the residue levels occurring in liver and milk of cows at the 1x dose rate in order to decide on necessity of MRL proposals | **DAS:** Noted | The calculated dietary burden accounted for 0.311 and 0.945 mg/kg in diet, respectively for dairy and beef cattle (see Addendum to the DAR – February 2007).<br>The 0.3 x treatment group (0.915 | PRAPeR 20 (27. – 30.03.2007):<br><br>Open point still open.<br><br>MRLs are likely to be necessary. See new |

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| | See reporting table 3(24). | | mg/kg in diet) – Table B.7.2.1-2 in DAR showed that the residue levels in liver and milk raised respectively 0.045 mg/kg and 0.008 mg/kg.<br>RMS -June 2007 :<br>According to the proposed residue definition for monitoring and the results of the ruminant feeding study present in the DAR (Table B.7.8.1-1), a MRL of 0.01* mg/kg can be proposed for milk, muscle, fat, liver and kidney. | data gap for a ruminant metabolism study.<br><br>Evaluation meeting (14-15.11.2007)<br>Open point still open. |
| | Open point 3.16<br>Inlcusion of RH-9090 in the residue definition for risk assessment triggers re-evaluation of residue data relevant for consumer intake assessment and assessment of livestock dietary burden (STMR, HR)<br>Revised calculations to be presented in an addendum<br>In that context it should be checked whether sufficient data on RH-9090 are available for risk assessment purposes (e.g. storage stability data, validated analytical data generation methods, processing data)<br>To be reported in an addendum. | **DAS:** Noted | All these points were discussed in the Addendum to the DAR – February 2007.<br>RMS -June 2007 :<br>Several analytical methods used for the determination of the residues of Myclobutanil and its alcohol metabolite RH-9090 were available and detailed in the DAR (B.7.6).<br>Only the following methods TR 34S-88-10 and DMK/03/01 had a methodology involving an acidic hydrolysis step to free any conjugated RH-9090.<br>The analytical methods/residue trials for apples and grapes are reported in the residue trials summary sheets in Appendix C to theDAR.<br>Considering the level of RH-9090 relative to Myclobutanil in both samples that were analysed using a hydrolysis | PRAPeR 20 (27. – 30.03.2007):<br><br>Open point fulfilled.<br><br>New data gap: The applicant should provide evidence that the submitted trials cover the residue definition for risk assessment in particular with regard to conjugates. It should be demonstrated that the method used would extract all the conjugate and that the hydrolysis step in the method gives an acceptable yield. |

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| | See reporting table 3(27). | | step as well as those analysed without hydrolysis, a relatively small potential increase in the livestock and consumer dietary risk assessment from use of an analytical method that includes a hydrolysis step to free conjugated RH-9090 would be expected. Indeed, when comparing results from samples analysed with no hydrolysis step to those where hydrolysis was used it does not seem to be a consistently large difference in the level of RH-9090 recovered (RH-9090 as a % of the myclobutanil level in the samples used for comparison from analysis with no hydrolysis ranged from 5.3% to 16.7% while the range for samples analyzed using a method with a hydrolysis step ranged from 13.8% to 20%). | |
| 3.3 | Data gap identified at PRAPeR 20:<br>The applicant should provide evidence that the submitted trials cover the residue definition for risk assessment in particular with regard to conjugates. It should be demonstrated that the method used would extract all the conjugate and that the hydrolysis step in the method | | RMS -June 2007 :<br>See open point 3.16 | PRAPeR 20 (27. – 30.03.2007):<br><br>Data gap open.<br><br>Evaluation meeting (14-15.11.2007)<br><br>Data gap open. |

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| | gives an acceptable yield. | | | |
| | Open point 3.17<br>Results of trials additionally accepted as valid by RMS to be presented in an addendum<br><br>Note: If higher residues occur at a later PHI than 14, these residues values have to be considered in the risk assessment.<br>RMS to review residue data accordingly<br><br>See reporting table 3(31). | **DAS:** Noted | The residue trials summary sheets are presented in the Addendum to the DAR – February 2007.<br>RMS -June 2007 :RMS agrees that additional residue trials in apples can be considered as valid at a later PHI than 14 days. These are detailed as follows and the summary sheets are included in the Addendum –June 2007 :<br>**North** :<br>Myclobutanil : 0.16-0.16-0.15 mg/kg<br>RH-9090 : <0.01-<0.01-0.03 mg/kg<br>Referring to the complete data base,<br>STMR -Myclobutanil: 0.15 mg/kg<br>Rmax -Myclobutanil : 0.335 mg/kg<br>Rber -Myclobutanil : 0.32 mg/kg<br>**South** :<br>Myclobutanil : 0.196 mg/kg<br>RH-9090 : 0.027 mg/kg<br>Referring to the complete data base,<br>STMR -Myclobutanil: 0.08 mg/kg<br>Rmax -Myclobutanil: 0.201 mg/kg<br>Rber -Myclobutanil: 0.258 mg/kg<br>The MRL proposal of 0.5 mg/kg for apple fruit remains unchanged. | PRAPeR 20 (27. – 30.03.2007):<br><br>Open point still open.<br><br>The residue data base for apples should be reconsidered accordingly.<br><br>Evaluation meeting (14-15.11.2007)<br><br>Not peer reviewed. Open point still open. |
| | Open point 3.18 | **DAS:** Noted | The residue trials summary sheets are presented in the Addendum to the DAR | PRAPeR 20 (27. – 30.03.2007): |

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| | Results of trials additionally accepted as valid by RMS to be presented in an addendum<br><br>Note: If higher residues occur at a later PHI than 14, these residues values have to be considered in the risk assessment.<br>RMS to review residue data accordingly<br><br>See reporting table 3(33). | | – February 2007.<br>RMS -June 2007 :RMS agrees that additional residue trials in grapes can be considered as valid at a later PHI than 14 days. These are detailed as follows and the summary sheets are included in the Addendum –June 2007:<br>**North** :<br>Myclobutanil : 0.33-0.29-0.20-0.05-0.10 mg/kg<br>RH-9090 : 0.02-0.01-0.02-<0.01-0.02 mg/kg<br>Referring to the complete data base,<br>STMR -Myclobutanil : 0.14 mg/kg<br>Rmax -Myclobutanil: 0.517 mg/kg<br>Rber -Myclobutanil: 0.59 mg/kg<br>**South** :<br>Myclobutanil : 0.08 mg/kg<br>RH-9090 : 0.03 mg/kg<br>Referring to the complete data base,<br>STMR -Myclobutanil: 0.06 mg/kg<br>Rmax -Myclobutanil: 0.15 mg/kg<br>Rber -Myclobutanil: 0.18 mg/kg<br>The MRL proposal of 1 mg/kg for grapes remains unchanged. | Open point still open.<br><br>The residue data base for grapes should be reconsidered accordingly.<br><br>Evaluation meeting (14-15.11.2007)<br><br>Not peer reviewed. Open point still open. |
| 3.1 | Data requirement<br>Studies simulating representative processing conditions to be submitted by | **DAS:** we confirm the announced deadline of **June 2007.** | RMS notes that further studies are announced for June 2007.<br>RMS -June 2007 : | PRAPeR 20 (27. – 30.03.2007):<br><br>Data requirement still open. |

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| | the applicant. This study should investigate the behaviour of the relevant residue (potentially including relevant metabolites) on crops to be processed.<br><br>The notifier indicated that a study will be conducted and the final report will be available by June 2007<br><br>See reporting table 3(37). | | The final report of the study : "Processing Study to Determine the Nature of residues of Myclobutanil Following Industrial or Household Preparation – Rotondaro S.L., 2007)" was received at the end of June 2007 and was evaluated by RMS. This is included in the Addendum to DAR – June 2007.<br>RMS concluded that Myclobutanil and its metabolite RH-9090 can be regarded as stable to hydrolysis. This conclusion was not peer reviewed. | Evaluation meeting (14-15.11.2007)<br>Data requirement still open. |
| | Open point 3.19<br>Addendum on transfer /processing factors is awaited.<br>Note: The discrepancy observed in terms of the apple pomace processing factors is easily explained by the fact that the factors 0.55 and 0.646 refer to apple puree rather than to apple pomace. (refer to p.16 and p.29 of the report)<br>Why is a residue study with a higher application rate not eligible to derive a processing factor? A sound argument should be provided for that | **DAS:** With regard to the acceptability of the trial in which a 5X application rate was used, this higher rate was included in the study in case residues were below the LOQ in some of the processed fractions with the 1X application rate. The concentration factor for pomace is essentially the same in the study for the 1X and 5X application rate, 2.87 and 3.07, respectively.<br><br>For the discrepancy in the processing factors: indeed the way the data are reported in the older report does not help: the two processed fractions are "Most", which we translated to juice / cider and ""Mus", which we translated | The transfer factors are presented under open point 3.16 (Table B.7.7.2-1) in the Addendum to the DAR – February 2007. | PRAPeR 20 (27. – 30.03.2007):<br><br>Open point fulfilled.<br>Processing factors in question are for juice and puree and not pomace. |

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| | decision.<br>However, final conclusion on processing is pending the outcome of the study on the effects on the nature of residues (data requirement)<br><br>See reporting table 3(38). | to pomace, no text in the report explains how the processing was carried out and how the "Mus" was produced and its exact identity / composition so indeed we cannot exclude that the correct translation is "Apple puree" as indicated by EFSA; in this case the results of the transfer factors for Mus in the older study compare reasonably well with the transfer factors for puree in the 2004 study (0.55 and 0.646 in the old study vs. 0.25 for puree in the 2004 study). | | |
| | Open point 3.20<br>Recalculation of livestock dietary burden under consideration of the relevant residues for risk assessment and valid processing factors to be presented in an addendum<br>Upon that recalculation the comparison to the dose rates in feeding studies and an estimation of potential residues in food of animal origin to be redone<br><br>See reporting table 3(41). | **DAS:** Noted | A) The livestock dietary burden calculation based on the new residue definition for risk assessment in apples and grapes is presented in the Addendum to the DAR – February 2007 under open point 3.16.<br>B) Considering the maximum dietary intake for beef cattle (0.945 mg/kg diet), the lower dosing group in the cow feeding study can be considered as an over-estimation of around 1.6 fold the actual residue level that may occur in the feeding stuffs. The residue level of the parent myclobutanil, the alcohol RH-9090 and the diol RH-294 are below the LOQ (0.01 mg/kg) of the analytical method in milk and in edible tissues of ruminants (Table | PRAPeR 20 (27. – 30.03.2007):<br><br>Open point still open<br><br>Livestock dietary burden needs to be recalculated in accordance with the agreements of the meeting.<br><br>Evaluation meeting (14-15.11.2007)<br>Not peer reviewed. Open point still open. |

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| | | | B.7.8.1-1 in the DAR).<br>RMS -June 2007 :<br>The revised livestock dietary burden calculation (Addendum to the DAR – March 2007) was based on the following residue definition for risk assessment : Myclobutanil + RH-9090 expressed as myclobutanil and considering the highest residue value of 0.38 + 0.02 mg/kg in apple fruit.<br>The transfer factor for wet pomace – 1.78- (DAR) is not correct. The correct value is 2.97.<br>The calculated dietary burden was amended with 0.494 mg/kg and 1.5 mg/kg diet, respectively for dairy and beef cattle and is included in the Addendum –June 2007.<br>The 1.6 ppm dose level used in the feeding study (B.7.8.1 in DAR) corresponds to the calculated dietary burden. The residues of Myclobutanil and RH-9090 in milk, muscle, fat, liver and kidney were below the Limit of Detection (0.003 mg/kg) (Table B.7.8.1-1 in DAR).<br>Therefore, any increase in dietary burden that might result from the use of an analytical method that includes a hydrolysis step would not be expected to increase the dietary burden to the point where the proposed MRL of 0.01* | |

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| | | | mg/kg for products of animal origin would need to be increased. | |
| | Open point 3.21<br>RMS to specify what "out of any toxicological relevance" means<br>(as toxic as myclobutanil?)<br><br>See reporting table 3(42). | **DAS:** Noted | The metabolite 4-hydroxy-3-lactone identified in cow liver and kidney was also recovered in the rat metabolism and is considered to have a similar toxicity as the parent compound.<br>This metabolite is "out of any toxicological relevance" since it is covered by all the available toxicological studies performed (see section mam tox). | PRAPeR 20 (27. – 30.03.2007):<br><br>Open point fulfilled.<br><br>See new data gap for a ruminant metabolism study. (data gap 3.2) |
| | Open point 3.22<br>While in metabolism study the diol metabolite RH294 was identified as a major metabolite, in the feeding study the carboxylic acid RH294 was anaylsed for. RMS to give further clarification on that issue.<br><br>See reporting table 3(42). | **DAS:** Noted | The metabolite RH-294 is a diol and not a carboxylic acid according to the proposed chemical structure.<br>RMS -June 2007 :<br>-In the metabolism study in lactating cows (point B.7.2.1 in DAR), it is confirmed that the metabolite RH-294 is the 4, 5-diol metabolite.<br>-A corrigendum must be addressed for the cow feeding study (DAR – B.7.8.1) regarding the reference to the metabolite RH-294 as a diol instead of a carboxylic acid metabolite.<br>In the DAR, in Table B.7.8.1-1, "Carboxylic acid RH-0294" in the first column must be read "4,5-diol RH-0294".<br>The text of the study report is correct | PRAPeR 20 (27. – 30.03.2007):<br><br>Open point fulfilled.<br>New data gap: A GLP amendment is required for the animal feeding study to address the reference to the carboxylic acid. |

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| | | | and there is no report revision needed.<br>This clarification removes the concern regarding a GLP correction of the study reports. | |
| 3.4 | Data gap identified at PRAPeR 20:<br>A GLP amendment is required for the animal feeding study to address the reference to the carboxylic acid. | | RMS -June 2007 :<br>See open point 3.22. | PRAPeR 20 (27. – 30.03.2007):<br><br>Data gap open.<br><br>Evaluation meeting (14-15.11.2007)<br>Data gap open.<br><br>Post meeting note by EFSA:<br>The erroneous naming of a compound was in the DAR and the summary dossier but not in the relevant study as previously indicated by the RMS. Therefore a GLP amendment is not required and the data gap could be closed.<br>The RMS should submit a corrigendum to the DAR. |
| | Open point 3.23<br>Given the long-life of myclobutanil residues in soil it should be checked with F&B section whether generation of soil metabolites that have not been found in plant | **DAS:** The only soil metabolite found at >5% was β-4-chlorophenyl-β-cyano-γ-(1H-1,2,4-triazole)butyric acid (referred to as the "butyric acid") which reached ca 6%. No other soil metabolites, including1,2,4-triazole, were seen. | Clarifications and a corrected statement are given in the Addendum to the DAR – February 2007.<br>RMS -June 2007 :<br>RMS disagrees to perform a new consumer risk assessment for the myclobutanil butyric acid metabolite. It | PRAPeR 20 (27. – 30.03.2007):<br><br>Open point still open. |

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| | metabolism may occur (e.g. trialzoles), and thus a potential uptake/accumulation of this compounds in plants following a repeated application (year by year) of myclobutanil might be expected<br><br>The statement in the DAR concerning the DT90 and non-requirement of studies is wrong and thus confusing and should be corrected in a revised DAR/corrigendum/addendum<br><br>See reporting table 3(44). | Regarding the myclobutanil soil DT90, the statement in the DAR should be corrected as the long DT90 values would normally trigger crop rotation studies. However, as has been noted previously, the planting of succeeding crops is not relevant in this case since both apples and grapes are long-lived crops that are not grown in rotation with other succeeding crops. | is not necessary for the following reasons :<br>-The butyric acid metabolite can be considered as a minor metabolite in soil (<6 % of AR),<br>-the concentration of this metabolite in ground water ranged between : 0.01-0.043 µg/L and 0.01-0.012 µg/L according to different methods of calculation used by RMS (F&B),<br>-this metabolite has no toxicological concern.<br><br>In that context, it has no sense to perform a risk assessment by comparing the concentrations of Myclobutanil butyric acid in ground water (drinking water) to the toxicological end points of the parent compound. | New open point: A consumer exposure assessment should be conducted for the myclobutanil butyric acid metabolite in ground water potentially used as drinking water.<br><br>Evaluation meeting (14-15.11.2007)<br><br>Open point still open. |
| | New open point 3.28: A consumer exposure assessment should be conducted for the myclobutanil butyric acid metabolite in ground water potentially used as drinking water. | | RMS -June 2007 :<br><br>See open point 3.23 | PRAPeR 20 (27. – 30.03.2007):<br><br>Open point open.<br><br>Evaluation meeting (14-15.11.2007)<br>Open point still open. |
| | Open point 3.24 | **DAS:** Noted | RMS presented a recalculation of the | PRAPeR 20 (27. – 30.03.2007): |

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| | RMS to present recalculation of NESTI under consideration of the relevant residues for risk assessment in an addendum<br>The addendum should include details on the calculations of the HR-P/ STMR-P values used in the NESTI calculations.<br><br>See reporting table 3(46). | | short term dietary risk assessment in the Addendum to the DAR – February 2007 under open point 3.16.<br>RMS -June 2007 :<br>A revised short-term dietary risk assessment was already performed in the addendum to the DAR-March 2007 considering the residue definition for risk assessment as Myclobutanil + RH-9090 expressed as myclobutanil.<br>The level of exhaustion of the ARfD value did not exceed 13%.<br>RMS agrees that this revised acute risk assessment is under estimated considering the following points :<br>-MRLs for ruminants matrices at the LOQ of the analytical method (0.01 mg/kg) should be included in the NESTI calculations considering the available metabolism and feeding studies in ruminants.<br>-the analytical method (method 310-84-13) associated with the residue trials generating the highest residue levels of myclobutanil and RH-9090 free in apples and grapes showed no evidence of a hydrolysis step performed on theRH-9090 conjugates to release RH-9090. Nevertheless, the use of a method including a hydrolysis step would be expected to result in relatively small increase in the total | Open point still open.<br><br>Evaluation meeting (14-15.11.2007)<br><br>Not peer reviewed. Open point still open. |

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| | | | residue level of Myclobutanil and RH-9090 in apples.<br>(see open point 3.16). | |
| | Open point 3.25<br>Procedural recoveries have to be at least 70%. In the light of that information RMS to review and report acceptable storage stability data in an addendum<br><br>See reporting table 3(47). | As was pointed out, the procedural recoveries for the 24 month time points for both the myclobutanil and the RH-9090 in almond hulls are just below 70% (67.1% and 66.5%, respectively). The 12 month procedural recoveries are at 66.3% for the RH-9090 in the almond hulls; but then at 18 months the procedural recoveries are again acceptable at 71.3% for the RH-9090 in the almond hulls. Recoveries are slightly low but are relatively consistent at each individual time point.<br><br>The procedural recovery for the 24 month time point for the RH-9090 in almond meat is below 70% (at 59.9%). The 18 month the procedural recovery for the myclobutanil in almond meat is 127% which exceeds the acceptability range and is out of line with the procedural recoveries obtained before and after that time point. However, recoveries are still relatively consistent at each individual time point.<br><br>The method seems to give relatively consistent recoveries at each individual time point, but it does not work very consistently from one time point to the | A conclusion regarding the storage stability of Myclobutanil and RH-9090 in almond hulls and meat is provided in the Addendum to the DAR – February 2007. | PRAPeR 20 (27. – 30.03.2007):<br><br>Open point fulfilled.<br>It could be concluded that residues of myclobutanil and RH-9090 are stable for at least 36 months. |

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| | | next. When the procedural recoveries are high so are the aged recoveries, and when the procedural recoveries are low then so are the aged recoveries. The recoveries for the aged samples vary in parallel with the procedural recoveries but that there is some inconsistency in the functionality of the method at different time points. When the procedural recoveries are used to correct the recoveries for the aged samples, the aged samples do not show any significant decline out to the 24 month time point and they are very consistent after correction. This supports the stability of myclobutanil and the RH-9090 out to 24 months. | | |
| | Open point 3.26<br>RMS to revise list of end points to reflect the respective STMR and HR values for the individual updated [as proposed in open points in 3(31) & 3(33)] data sets for N-EU and S-EU. The more critical data set is the one for N-EU.<br><br>See reporting table 3(51). | **DAS:** Noted | These new acceptable data will be included in the updated version of the LoEPs.<br>RMS -June 2007 :<br>The LoEPs has been amended accordingly. | PRAPeR 20 (27. – 30.03.2007):<br><br>Open point closed.<br><br>see new open point 3.29 |
| | Open point 3.27<br>RMS to present recalculation | **DAS:** Noted | RMS presented a recalculation of the chronic dietary risk assessment in the | PRAPeR 20 (27. – 30.03.2007): |

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| | of chronic intakes under consideration of the relevant residues for risk assessment and revised residue endpoints in an addendum<br><br>See reporting table 3(53). | | Addendum to the DAR – February 2007 under open point 3.16.<br>RMS -June 2007 :<br>The revised chronic intake was included in the addendum to the DAR-March 2007.<br>The level of exhaustion of the ADI value was below 10 % for the European adult consumer, accounted for 32% for the german girl and rose up to 9 % for UK toddlers.<br>Considering the updated residue data sets for N-EU and S-EU for both apples and grapes (see open points 3.17 and 3.18), the HR values for Myclobutanil remained unchanged while the STMR values for myclobutanil for both apples and grapes were not significantly modified.<br>RMS agrees that this revised chronic risk assessment is under estimated considering that the MRLs for ruminants matrices at the LOQ of the analytical method (0.01 mg/kg) should be included in the chronic intake calculations considering the available metabolism and feeding studies in ruminants.<br>With regards to the level of RH-9090relative to Myclobutanil in both samples that were analysed using a hydrolysis step as well as those | Open point still open.<br><br>Evaluation meeting (14-15.11.2007)<br><br>Not peer reviewed. Open point still open. |

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| | | | analysed without hydrolysis, a non significant increase in the STMR values from the use of an analytical method that includes a hydrolysis step to free conjugated RH-9090 would be expected (see open point 3.16). | |
| | Message to tox, residues, fate and ecotox that the technical material is a racemic mixture and has this been considered in the risk assessment. | | | PRAPeR 20 (27. – 30.03.2007):<br><br>New data gap: The applicant should address the risk assessment with regard to the isomers. |
| | Data gap identified at PRAPeR 20:<br><br>The applicant should address the risk assessment with regard to the isomers. | | RMS -June 2007 :<br>In the production process, neither stereo selective reaction types nor enantiomerically pure active substance are used. The Myclobutanil obtained is a racemic mixture (50:50 mixture of the 2 possible optical isomers).<br>All toxicological and residue metabolism studies were performed on the racemic mixture of the optical isomers. Provided the racemic mixture is stable the concern is covered by the tests performed. | PRAPeR 20 (27. – 30.03.2007):<br><br>Data gap open.<br><br>Evaluation meeting (14-15.11.2007)<br>Data gap open. |
| | New open point 3.29:<br><br>RMS to amend the list of end | | RMS -June 2007 :<br>The list of end points has been amended accordingly. | PRAPeR 20 (27. – 30.03.2007):<br><br>Open point open. |

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| | points as indicated in the discussion table. | | | Evaluation meeting (14-15.11.2007)<br><br>Open point fulfilled. |

## 4 Environmental fate and behaviour

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| | Section 4<br>Data requirements: ***3***<br>Open points: ***6*** | | | Section 4<br>Data requirements: ***1***<br>Data gap: ***1***<br>Open points:***1*** |
| | Open point 4.1<br>Meeting of experts to confirm that the available soil photolysis study is not reliable, then subsequently discuss if a new soil photolysis study should be required to complete the risk assessment for this substance, or not. The absence of significant absorption by myclobutanil above 290nm is important information for this discussion.<br><br>See reporting table 4(3). | **DAS:** Whilst some limited degradation occurred under the conditions of the soil photolysis study, this used continuous irradiation (and not a light/dark cycle) at 34ºC (higher than the nominal 20ºC recommended by SETAC). In fact, the slightly enhanced degradation seen in the photolysed samples compared to the dark controls at 30 days could be due to temperature effects. This is because the dark controls were covered in foil to exclude light, which would probably mean they were incubated at a lower temperature than 34°C. Furthermore, myclobutanil is not applied directly to soil, but is used as a foliar application in apple orchards and vineyards. This would limit exposure to soil, as indicated by 60-70% FOCUS crop interception values.<br>In conclusion, these points, when considered in conjunction with the fact that myclobutanil does not absorb above 290 nm, indicate that soil photolysis would not be expected to be | As RMS we confirmed that photolysis is not a significant route of degradation in the environment. As such, further investigation of this potential route of degradation in a new study is not considered necessary. | PRAPeR 17 (19. – 23.03.2007):<br><br>Open point fulfilled. |

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| | | a significant route of degradation in the environment. As such, further investigation of this potential route of degradation in a new study is not considered necessary. | | |
| | Open point 4.2<br>EFSA requests the endpoints should state: ‚for the representative uses evaluated (summer application to fruit crops)'<br><br>See reporting table 4(8). | **DAS:** Noted | As already indicated in the review report, we do not agree with this EFSA request. | PRAPeR 17 (19. – 23.03.2007):<br><br>Open point stays open.<br>RMS to update the list of endpoints anaerobic box to state not required for the representative use on grapes, data required for the use on apples.<br>A new data gap is identified.<br><br>Evaluation meeting (14-15.11.2007)<br>Open point fulfilled |
| | Data gap<br>A laboratory doil degradation study under anaerobic conditions is required for the representative use on apples. | | | PRAPeR 17 (19. – 23.03.2007):<br><br>Data gap open.<br><br>Evaluation meeting (14-15.11.2007)<br>Data gap open |
| | Open point 4.3<br>Please clarify in the endpoints if the lab studies method of DT50 calculation were estimated by linear or non linear regression (first | **DAS:** The DT50 values, both laboratory and field, were calculated using first-order kinetics and non-linear regression analysis. | The listing of endpoints has been amended. | PRAPeR 17 (19. – 23.03.2007):<br><br>Open point fulfilled. |

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| | order).<br><br>See reporting table 4(9). | | | |
| | Open point 4.4<br>LoEP soil adsorption/desorption to be updated to state there is no clear pH dependence of soil adsorption.<br><br>As the final RMS, UK and EFSA (see comment at line 4 (15)) conclusion is there is no clear evidence of pH dependance, RMS to to consider stating this position in a corrigendum or amended DAR.<br><br>See reporting table 4(13). | **DAS:** Noted | The listing of endpoints has been amended. | PRAPeR 17 (19. – 23.03.2007):<br><br>Open point fulfilled. |
| | Open point 4.5<br>RMS to add the second longer whole system single first order DT50 of 838 days to the endpoints sheet with an indication that the value is an uncertain estimate extrapolated significantly beyond the end of the study | **DAS:** Noted | The listing of endpoints has been amended. | PRAPeR 17 (19. – 23.03.2007):<br><br>Open point fulfilled. |

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| | See reporting table 4(24). | | | |
| 4.1 | Data requirement<br>FOCUSsw simulations at step 3 and 4 to be repeated for a single application for each intended use as these simulations are expected to give the highest PECsw concentrations appropriate for the short term risk assessment to free living aquatic organisms.<br><br>The applicant has indicated that the data have been sent to the RMS (December 2006).<br><br>See reporting table 4(29). | **DAS:** Noted | The new simulations are included in the addendum. | PRAPeR 17 (19. – 23.03.2007):<br><br>Data requirement fulfilled. |
| 4.2 | Data requirement<br>FOCUSsw simulations (step 4) to be repeated for the multiple application pattern for each crop of the intended use to account for potential | **DAS:** Noted | The new calculations are included in the addendum. | PRAPeR 17 (19. – 23.03.2007):<br><br>Data requirement fulfilled. |

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| | accumulation from use in successive years as outlined in section 8.7.3 page 217 of SANCO/4802/2001 rev.2 final (May 2003), as these simulations are expected to give the PECsw concentrations appropriate for assessing the long term risk assessment to free living aquatic organisms and will give the highest PECsediment required to complete the sediment dweller risk assessment.<br><br>The applicant has indicated that the data have been sent to the RMS (December 2006).<br><br>See reporting table 4(31). | | | |
| | Open point 4.6<br>RMS to prepare an addendum to clarify:<br>- the kinetic formation fraction that was used in the PECgw calculation for myclobutanil butyric acid.<br>- the butyric acid DT50 for | **DAS:** Noted | The DAR has been updated. | PRAPeR 17 (19. – 23.03.2007):<br><br>Open point fulfilled.<br>(see data requirement 4.3) |

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| | each of the 4 soils at experimental and then FOCUS reference conditions with the normalisation calculations used explained.<br>- what the difference in the input values (application timing and crop interception) used to produce the 'realistic case and worst case' results reported were.<br><br>See reporting table 4(32). | | | |
| 4.3 | Data requirement<br>Applicant to provide new groundwater modelling for myclobutanil and myclobutanil butyric acid ensuring the FOCUS reference condition DT50 for myclobutanil butyric acid is correctly calculated in line with FOCUS guidance (the EFSA calculated this DT50 to be 15.6 days) and the formation fraction of butyric acid from myclobuanil used in modelling is clearly reported and reflects FOCUS guidance. Modelling to use FOCUS PEARL in addition to | **DAS:** Noted | The new PEC calculations are included in the addendum | PRAPeR 17 (19. – 23.03.2007):<br><br>Data requirement maintained<br><br>Derivation of normalised field DT50 values employed need to be transparently presented.<br>PEC GW need to be recalculated with appropriate kinetic formation fractions for metabolite myclobutanil butyric acid.<br>The new modelling should use the correct normalized DT50 values for metabolite myclobutanil butyric acid.<br>Two FOCUS models (following the EFSA PPR panel Opinion) should be used with the appropriate input parameters.<br>For myclobutanil butyric acid if Kd is used |

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| | FOCUS PELMO or FOCUS PRZM.<br>The applicant has indicated that the data have been sent to the RMS (December 2006).<br><br>See reporting table 4(33). | | | 1/n should be 1 and not 0.9.<br><br>Evaluation meeting (14-15.11.2007)<br>Data requirement maintained |
| | New open point 4.7:<br><br>RMS to amend the list of end points according to the discussion table | | **June 2007**<br><br>The listing of endpoints has been amended.<br>See letter in attachment | PRAPeR 17 (19. – 23.03.2007):<br><br>Open point open.<br><br>Evaluation meeting (14-15.11.2007)<br>Open point remains open<br>Individual $K_F$oc / Kdoc values was not added to the LoEP as requested in the meeting of experts (only the range is given). |

## 5 Ecotoxicology

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| | Section 5<br>Data requirements: ***2***<br>Open points: ***14*** | | | Section 5<br>Data requirements: ***1***<br>Data gaps: ***1***<br>Open points: ***5*** |
| | Open point 5.1<br>The issue of risk to birds and mammals from intake of contaminated drinking water is still under debate and will be further addressed in the revised Guidance document. For the mean time it is proposed that issue is dicussed in the experts' meeting.<br><br>See reporting table 5(2). | **DAS:** Noted that this point is still under debate. | **RMS (February 2007) :**<br>No comment.<br>**RMS (June 2007) :**<br>The calculations for acute exposure to drinking water are presented in update June 2007 of VOL3(B9). | PRAPeR 18 (19. – 23.03.2007):<br><br>Open point fulfilled. |
| | Open point 5.2<br>RMS to clarify how the residue unit value (RUD) of 22.8 in the refinement was derived and to calculate a long-term TER for mammals for the use of myclobutanil in apples with 2 applications during flowering (65% interception) and 2 applications at a stage when | **DAS:** we confirm the RMS explanation in the "comments received on reporting table" at 5(3). | **RMS (February 2007) :**<br>RUD = 22.8 = 30 % of 76<br>(clearly stated in the DAR)<br>The refined long-term risk assessment for mammals will be presented in update March 2007 of VOL3(B9).<br>**RMS (June 2007) :**<br>The refined long-term risk assessment for mammals for the use in apples with 2 applications during | PRAPeR 18 (19. – 23.03.2007):<br><br>Open point still open.<br><br>Evaluation meeting (14-15.11.2007)<br><br>Open point closed. |

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| | foliage is developed (70% interception) in an addendum.<br><br>See reporting table 5(3). | | flowering and 2 applications during foliage development is presented in update June 2007 of VOL3(B9). | |
| | Open point 5.3<br>To be discussed in an expert's meeting if the endpoint values for acute and short term should be corrected for the low content of a.s.<br>For the evaluated uses the outcome of the risk assessment would not be changed.<br><br>See reporting table 5(4). | **DAS:** Oral and dietary doses were calculated based on the 84.5% purity of the technical material. Therefore the reported doses are corrected for purity and results are reported as mg as/kg. This makes them applicable to any risk assessment situation irrespective of technical specification | **RMS (February 2007) :**<br>RMS agrees with the statement of the notifier, considering the endpoints :<br>$LD_{50}$ = 510 mg a.s./kg b.w.<br>$LC_{50}$ > 567 mg a.s./kg b.w./day<br>$LC_{50}$ > 1544 mg a.s./kg b.w./day<br>and the acceptable TER values.<br>For the evaluated uses the outcome of the risk assessment would not be changed. | PRAPeR 18 (19. – 23.03.2007):<br><br>Open point fulfilled. |
| 5.1 | Data requirement:<br>Notifier to calculate the $E_rC_{50}$ from the study with *Scenedesmus subspicatus* (Ellgehausen, 1987).<br><br>The applicant has indicated that the data have been sent to the RMS (December 2006). | **DAS:** the calculated ErC50 from the study with *Scenedesmus subspicatus* (Ellgehausen, 1987) is available. Growth rate was calculated for the periods of 0-72 and 0-96 hours using mean cells/mL for each treatment and for the pooled control. **Linear regression was used to calculate the ErC50 values based on nominal concentrations which were 7.5 mg/L for 72-hours and 6.7 mg/L for 96-hours.** | **RMS (February 2007) :**<br>The endpoints for $E_rC_{50}$ are added in update March 2007 of VOL3(B9). | PRAPeR 18 (19. – 23.03.2007):<br><br>Data requirement fulfilled. |

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| | See reporting table 5(7). | | | |
| | Open point 5.4<br>Experts' meeting to discuss whether a BCF study is necessary<br><br>See reporting table 5(10). | **DAS:** the Notifier prepared the following position Document based on the Guidance Document on Aquatic Ecotoxicology (SANCO/3268/2001 rev.4 (final) 17 October 2002:<br><br>"*Risk Assessments for Myclobutanil Considering Potential Log Kow and BCF Values*", (sent to the RMS in December 2006).<br><br>With this Risk Assessment it has been shown that even with the predicted log Kow of 3.50, the BCF for myclobutanil is likely to be <100. Therefore, a BCF study with fish is not triggered. Risk assessments show acceptable risk to fish and fish-consuming birds and mammals using the BCF calculated from a predicted log Kow of 3.50. Risk assessments also show acceptable risk to fish and fish-consuming birds and mammals even in the unlikely case that the BCF is 1000 when myclobutanil is used according to the proposed application rates. There is no concern for biomagnification in aquatic food chains according to triggers defined in the Guidance Document on Aquatic Ecotoxicology. Given the positive results of these extreme worst-case risk assessments, a BCF study with myclobutanil is not necessary. | **RMS (February 2007) :**<br>The experimentally determined<br>log $P_{OW}$ value = 2.56,<br>the calculated<br>log $P_{OW}$ value = 2.89<br>and the modelled<br>log $P_{OW}$ value = 3.50<br>the newly experimentally determined<br>log $P_{OW}$ value = 3.17<br><br>Very likely the log $P_{OW}$ is around 3 and it is up to the meeting to decide whether a BCF study is required. | PRAPeR 18 (19. – 23.03.2007):<br><br>Open point fulfilled.<br><br>Data gap identified:<br>Notifier to provide a BCF study in fish. |

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| | | The complete document is attached to the Evaluation Table as word file:<br><br>**Appendix I** to Evaluation Table **section 5**<br><br>As reported at point 1(7) of the Reporting Table a new log Pow test will be conducted using shake flask method and including information on phase separation. The report will be available by the **end of February 2007**. | | |
| 5.3 | Data gap identified at PRAPeR 18:<br>Notifier to provide a BCF study in fish. | | **RMS (June 2007) :**<br>No comment. | PRAPeR 18 (19. – 23.03.2007):<br><br>Data gap open<br><br>Evaluation meeting (14-15.11.2007)<br><br>Data gap open |
| | Open point 5.5<br>The reporting of the risk assessment for aquatic organisms to be discussed in an experts' meeting.<br><br>See reporting table 5(11). | **DAS:** Noted | **RMS (February 2007) :**<br>The aquatic risk assessment is reported according to EPCO No E 4, revision 4 (September 2005) manual in update March 2007 of VOL3(B9). | PRAPeR 18 (19. – 23.03.2007):<br><br>Open point fulfilled. |

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| | Open point 5.6<br>The use of TWA $PEC_{sw}$ in the risk assessment for aquatic organisms to be discussed in an experts' meeting.<br><br>See reporting table 5(12). | **DAS:** The risk assessments presented in the dossier clearly show that the results for FOCUS steps 1 and 2 do not pass the risk assessments. Therefore, Step 3 and 4 mitigations are needed. FOCUS methodology stipulates different buffer zones for different water bodies as part of the standard FOCUS procedures. Please refer to FOCUS guidance for information. The use of time weighted average concentration for the chronic TER calculations is appropriate since the fathead minnow test was conducted as a flow-through test the Daphnia chronic test was a static-renewal test. In each instance the measured concentrations were >80% of the nominal concentrations during the tests and the toxicity values were based on nominal concentrations. The time to onset of effects for each study was the entire study period since the NOEC for the fathead test was based on final fish length and the NOEC for the Daphnia test was based on reproduction over the entire test period. | **RMS (February 2007) :**<br>The use of TWA $PEC_{SW}$ for the chronic risk assessment is justified according to SANCO/3268/2001.<br>There was an unrealistic exposure regime in the relevant toxicity tests :<br>*O. mykiss* : 21 d flow-through<br>*D. magna* : 21 d semi-static<br>**RMS (June 2007) :**<br>The revised chronic risk assessment based on initial $PEC_{SW}$ values, as agreed in the PRAPeR meeting, is presented in update June 2007 of VOL3(B9). | PRAPeR 18 (19. – 23.03.2007):<br><br>Open point still open.<br><br>Evaluation meeting (14-15.11.2007)<br>Open point closed |
| | Open point 5.7<br>MS to discuss the risk to sediment dwelling organisms with focus on<br>• Conversion of NOEC | **DAS:** The risk assessment prepared by DAS in the dossier for the exposure of sediment dwelling organisms has been performed by comparing the chronic NOEC value of *Chironomus riparius* with | **RMS (February 2007) :**<br>The risk of myclobutanil to sediment dwelling organisms is based on the NOEC = 4.98 mg a.s./L<br>and max $PEC_{SW}$ initial. | PRAPeR 18 (19. – 23.03.2007):<br><br>Open point still open.<br><br>Evaluation meeting (14-15.11.2007) |

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| | water to NOEC sediment<br>• Use of mean NOEC value (mean of concentration in sediment)<br>• Use of TWA PEC sediment versus plateau level (see comment 4(31)<br>The risk from the representative uses seem to be low, but the assessment should be discussed from a general point of view.<br><br>See reporting table 5(13). | the global maximum predicted environmental concentration in surface water. In this instance the PECsw is used instead of the $PEC_{SED}$ because the test design for the chironomid 31-day chronic test used a water dose and not a sediment dose. The RMS converted the NOEC based on the water dose level of 5 mg a.s./L to the equivalent measured TWA of the sediment concentration, 10 mg a.s./kg. The TWA was used because the sediment concentration varied over the duration of the study, as one would expect in a water-dosed system. Comparing this value to the comparable TWA PEC is appropriate, as this PEC simulates a similar exposure pathway, that is, water "dosed" by spray drift deposition followed by partitioning to bed sediment. Both approaches in the risk assessment, either comparing global max. PECsw to the NOEC expressed in mg/L, or comparing TWA PECsed to the TWA NOEC expressed in mg/kg, demonstrate safe use. | The corrections are made in update March 2007 of VOL3(B9) and in the List of Endpoints.<br>**RMS (June 2007) :**<br>The calculations based on the toxicity and exposure in sediment, as agreed in the PRAPeR meeting, are presented in update June 2007 of VOL3(B9). | Open point closed. |

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| | Open point 5.8<br>The choice of chronic endpoint for fish to be discussed in an experts' meeting.<br><br>See reporting table 5(14). | **DAS:** Noted | **RMS (February 2007) :**<br>NOEC (*O. mykiss*, 21 d) = 0.2 mg a.s./L<br>NOEC (*P. promelas*, 35 d) = 0.98 mg a.s./L<br>The choice of the chronic endpoint for fish will not alter the risk assessment. | PRAPeR 18 (19. – 23.03.2007):<br><br>Open point fulfilled. |
| | Open point 5.9<br>RMS to clarify whether FOCUS modelling using a single application (with the resulting higher spray drift %) did not result in higher global maximum PECsw than the multiple application simulations currently reported, and if necessary to correct the TER calculations using the highest global max values.<br><br>See reporting table 5(16). | **DAS:** The data for the single application scenario have been sent to the RMS (December 2006), see Data Requirement 4.1. | **RMS (February 2007) :**<br>The $PEC_{SW}$ and $PEC_{SED}$ for single application pattern have been calculated considering the assumptions used for the previous PEC calculations. Considering the very high uncertainty related to the FOCUS PEC surface water simulations, the results of both PEC calculations (single or multiple applications) are similar. We consider therefore that it is more appropriate to base the TER calculations on the PEC multiple applications. Moreover, the risk assessment shows that the risk for aquatic organisms is acceptable with rather easily feasible mitigations measures (short buffer zones). | PRAPeR 18 (19. – 23.03.2007):<br><br>Open point still open.<br><br>Evaluation meeting (14-15.11.2007)<br><br>Open point closed |

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| | Open point 5.10<br>The list of end points has been updated to include worst case scenario and water body type. However, it is proposed to discuss the presentation of the risk assessment for aquatic organisms in an experts' meeting as a general point.<br><br>See reporting table 5(17). | **DAS:** Noted | **RMS (February 2007) :**<br>Please refer to open point 5.5. | PRAPeR 18 (19. – 23.03.2007):<br><br>Open point fulfilled. |
| | Open point 5.11<br>The field study conducted with *Typhlodromus pyri* to be discussed in an experts' meeting.<br><br>See reporting table 5(23). | **DAS:** the RMS acknowledges low PREDATORY mite populations at the beginning of the study and that populations increased during the study until the start of autumn when the mite population fell into a natural period of seasonal decline. Low numbers are normal for mite populations in field trials started in the spring. Populations are not static. Population numbers were similar for all treatments during the respective sampling dates. The PREDATORY mite numbers were sufficient for evaluation. Predatory mite populations in the positive control were never greater than in the untreated controls during the study. Prior to the 5th application there was 66.5% negative effect on the positive control mites and the effect increased to 88.5% | **RMS (February 2007) :**<br>Indeed, mite populations were low at start but increased during the study for the untreated control. We consider that the study is valid (n° of replicates, observation on the predatory mites and spider mites).<br>Moreover, this study has been performed at the application rate of 9 x 90 g a.s./ha and 9 x 180 g a.s./ha, while the maximum application rate in apple is 4 x 90 g a.s./ha. | PRAPeR 18 (19. – 23.03.2007):<br><br>Open point fulfilled. |

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| | | 4 weeks after the last application. This is not poor performance by propineb. PEST spider mite populations are low in the study in the control treatment. In the toxic reference plots the PEST mites were high in mid summer and remained high until the end of the trial. These Pest mites are prey for the PREDATORY mites studied in this trial. The reason for the increase and high occurrence of PEST mites in the toxic reference treatment was due to the adverse effects on the PREDATORY mites leading to reduced predation. We consider the study is valid and reliable. | | |
| | Open point 5.12<br>The risk to NTA to be discussed in an experts' meeting and in particular the need for further studies with crop relevant species.<br><br>See reporting table 5(24). | **DAS:** Extended laboratory and field studies on the sensitive species *A. rhopalosiphi, T. pyri and C. carnea* indicate acceptable risk at rates ≥3x the annual field rate for orchards. The *C. septempunctata* study, when interpreted in the guidance of ESCORT 2 does not indicate risk to NTAs at the rate of 36 g a.s./ha tested. In the study a correct mortality for ladybird larvae of 11.9% was observed, which is below the ESCORT 2 trigger of 50% effects. In the reproduction phase of the study, females in the control groups produced a mean of 6.46 eggs/female whereas in the Systhane treatment females produced a slightly lower number of 4.07 | **RMS (February 2007) :**<br>Please refer to update March 2007 of VOL3(B9). | PRAPeR 18 (19. – 23.03.2007):<br><br>Open point fulfilled. |

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| | | eggs/female. In effect terms this is equal to a 37% reduction compared to the control, which is below the ESCORT 2 trigger. In terms of hatching rate both treatments were similar. Due to high species-inherent variability it is now the custom to perform only a qualitative assessment of reproductive effects and it is the position of DAS that exposure to Systhane did not affect the reproductive performance of *C. septempunctata* and no further evaluation is necessary.<br>The potential risk to crop relevant species has been sufficiently addressed by studies with *C. septempunctata* and *C. carnea*. Together with the other valid higher tier studies with the sensitive indicator species *T. pyri* and *A. rhopalosiphi* it is the position of DAS that the risk to non-target arthropods has been fully considered and addresses the risk assessment requirement for the Annex I listing of myclobutanil. | | |
| | Open point 5.13<br>The suitability of the litter bag study by Mallet (2004) to address the risk to OM breakdown to be discussed in an experts meeting.<br><br>See reporting table 5(29). | **DAS:** The first study was not considered valid because soils were not measured for the test substance to confirm exposure and the study was based on an obsolete guideline. The second study followed the EPFES 2002 Guideline which does not require a positive control, but which does require residue analysis | **RMS (February 2007) :**<br>Please refer to update March 2007 of VOL3(B9). | PRAPeR 18 (19. – 23.03.2007):<br><br>Open point fulfilled. |

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| | | to confirm exposure. Test substance concentrations were measured in the second study and the values confirmed proper dosing following the Guideline recommendations. The dossier presents risk assessments based on the litterbag studies | | |
| | Open point 5.14<br>The issue of potential for endocrine disruption and whether further studies should be required (e.g. fish full life cycle study) to be discussed in an experts' meeting.<br>The risk to mammals should be revisited following the outcome of the discussions in the section mammalian toxicology.<br>See reporting table 5(42). | **DAS:** we agree with the statement in column 3 of the reporting table. Also, Results from acute and chronic studies of the effects of myclobutanil on birds, mammals, terrestrial invertebrates and aquatic organisms do not indicate endocrine disruption. Risk assessments indicate acceptable risk to non-target species groups with proper mitigation. Therefore, the risk of endocrine disruption from residues of myclobutanil is also acceptable. | **RMS (February 2007) :**<br>The possible endocrine effects are taken into consideration by the reproduction studies in setting a NOEC. Therefore we consider that this issue is addressed.<br>**RMS (June 2007) :**<br>From the section on mammalian toxicology, it was concluded that sufficient information is available to conclude on a safe use. | PRAPeR 18 (19. – 23.03.2007):<br><br>Open point still open.<br><br>Evaluation meeting (14-15.11.2007)<br><br>Open point closed for mammals, however potential endocrine effects for birds and fish are not addressed..<br><br>Data gap for the applicant to submit information to address potential endocrine effects in birds and in fish in particular since myclobutanil belongs to the group of triazole fungicides. |

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| 5.2 | Data requirement:<br>Applicant to submit information to address Annex II point 8 (vi).<br><br>The applicant has indicated that the information will be submitted to the RMS by end of December 2006<br><br>See reporting table 5(43). | **DAS:** the available information was sent to RMS on January 8th 2007. | **RMS (February 2007) :**<br>Please refer to addendum VOL4(C1-C2) of March 2007. | PRAPeR 18 (19. – 23.03.2007):<br><br>Data requirement still open.<br><br>Evaluation meeting (14-15.11.2007)<br><br>Data requirement still open. |